

C L A I M S

1. A method for modifying a wild strain of an entero-invasive Shigella to produce a modified strain of Shigella that can be used for making a vaccine against the wild strain of Shigella characterized by the step of transforming the genome of the wild strain of Shigella so that it cannot substantially invade cells of a host and cannot spread substantially within infected cells and from infected to uninfected cells of the host and cannot produce toxins which will kill substantial numbers of the host's infected, as well as uninfected, cells.
2. The method of claim 1 in which the genome of the wild strain of Shigella is modified so that a first gene, coding for a protein necessary for the wild strain of Shigella to invade cells, as well as tissues, of the host, and a second gene, coding for a protein necessary for the wild strain of Shigella to spread within infected cells and between infected and uninfected cells of the host, are wholly or partly removed or permanently inactivated.
3. The method of claim 2 in which the Shigella is an S. flexneri and the first gene codes for the production or use of aerobactin by the S. flexneri.
4. The method of claim 3 in which the second gene codes for intra-intercellular spread.
5. The method of claim 2 in which the Shigella is an S. dysenteriae 1, the genome of which is modified so that a third gene, coding for the production or use of Shiga-toxin by the S. dysenteriae 1, is wholly or partly removed or permanently inactivated.
6. The method of claim 5 in which the first gene of the S. dysenteriae 1 codes for the production or use of enterochelin by the S. dysenteriae 1.

7. The method of claim 6 in which the second gene codes
for intra-intercellular spread.
- 5 8. The method of claim 6 in which the first gene
comprises the ent F, Fep E, Fep C and Fep D subunit genes
of the enterochelin operon of the S. dysenteriae 1.
9. The method of anyone of claims 5-8 in which the first,
second and third genes are mutagenized.
- 10 10. The method of anyone of claims 2-9 in which one or
more of the genes are inactivated by allelic exchange
with one or more in vitro mutagenized genes, especially
mutagenized genes from which significant portions have
been deleted and particularly mutagenized genes into
15 which marker genes have been inserted.
11. A Shigella which has been modified by the method of
anyone of claims 1-10 or is a descendant thereof.
12. A vaccine which has been made from the modified
Shigella of claim 11.
- 20 13. A Shigella which is Shiga-toxin, particularly
Shiga-toxin A.

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